

CASE CT2605 NP

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Maureen S. Gibbons

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March 22, 2004

Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

Art Unit: 1621

ERICSSON ET AL.

Examiner: Paul A. Zucker

APPLICATION NO: 10/075,845

FILED: FEBRUARY 13, 2002

FOR: COMPOUNDS HAVING RETINOID-LIKE ACTIVITY

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPELLANTS' BRIEF PURSUANT TO 37 C. F. R. § 1.192

Applicant appeals the Final Rejection dated July December 23, 2003 in connection with the above-identified patent application.

I. Real Party in Interest

The real party in interest in the above-identified patent application is Bristol Myers Squibb Company, a corporation in Delaware, which is the assignee of Anna Ericsson, Anne Marinier, and Fred C. Zusi.

II. Related Appeals and Interferences

There are no pending appeals or interferences known to appellants or the appellants' assignee, which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. Status of the Claims

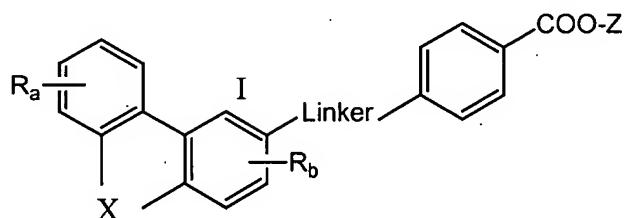
Claims 1 to 3, 5, and 10 to 12 are pending, claims 4, 6 to 9, and 13 to 20 have been cancelled pursuant to a restriction requirement. Claims 1 to 3 and 5 stand finally rejected and form the subject of the appeal. Claims 10 to 12 are objected to as depending from rejected claims.

IV. Status of Amendments

An amendment filed on January 4, 2004, subsequent to the final office action was entered.

V. Summary of Invention

The present invention is directed to compounds having the formula:



or a nontoxic pharmaceutically acceptable salt, physiologically hydrolyzable ester or solvate thereof, wherein

R_a and R_b are independently selected from the group consisting of hydrogen, halogen, hydroxy, nitro, amino, substituted amino, mercapto, polyfluoroalkyl, C_{1-6} alkyl, substituted C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylthio, formyl, carboxyl, aryl or heteroaryl;

Linker is selected from the group consisting of C_2 alkyl, C_2 alkenyl, C_2 alkynyl, $--C(=O)-NH--$, $--NH-C(=O)--$, $--CH_2O--$, $--O-C(=O)--$, $--C(=S)-NH--$, $--C(=O)-O--$, $--C(=O)-S--$, $--S-C(=O)--$, $--S-CH_2--$, $--CH_2-NH--$, $--C(=O)-CH_2--$, $--NH-C(=S)--$, $--CH_2S--$, $--OCH_2--$, $--NHCH_2--$;

X is O , S , $-C(R_1)_2$, $C=O$, $-C(R_1)_2Y--$ or $--YC(R_1)_2--$, wherein Y is selected from the group consisting of O , S and $C(R_2)_2$, wherein R_1 and R_2 are, independently, hydrogen or methyl; and

Z is hydrogen or C_{1-6} alkyl.

The compounds of the present invention are useful for the treatment of cancer and other related disorders. The activity of the compounds of the present invention are similar to the known class of compounds, retinoids. Retinoids have been shown to affect

cellular growth and differentiation and are promising drugs for the treatment of several cancers. See, for example, Roberts, A. B. and Sporn, M. B. in "The Retinoids," Sporn, *et al.* eds, 1984, 2, pp. 209-286, Academic Press, New York; Lippman, *et al.*, *Cancer Treat. Rep.*, 1987, 71, p. 391; *ibid.*, p. 493; Hong *et al.*, *N. Engl. J. Med.*, 1990, 323, p. 795; Huang, M. *et al.*, *Blood*, 1988, 72, p. 567. The compounds of the present invention compare very favorably to known retinoids in three assay systems, including a competition binding assay, a transactivation assay, and a growth assay. See, specification, pages 44 to page 45 line 7. However, the compounds of the present invention have significantly enhanced inhibition against two tested cell lines. Without wishing to be bound by any particular theory, it is believed that the compounds of the present invention are more stable metabolically than the relatively labile retinoic acid, and that their greater persistence is the cause of their greater activity.

VI. Issue

Whether U.S. Pat. No. 5,075,487 (the '487 patent) which discloses intermediates that are useful in making electron transport materials for use in multilayered electrophotographic photoreceptors may be used by the examiner in rejecting the claims as obvious in view of the '487 patent under 35 U.S.C. § 103 (a)?

VII. Grouping of the Claims

Appellant believes that claims 1 to 3 and 5 stand or fall together.

VIII. Argument

The Rejection under 35 U.S.C. § 103 (a) is Improper

Because the reference cited in support of the obviousness rejection does not qualify as analogous prior art and because the examiner did not consider the anticancer activity possessed by the compounds of the present invention as relevant to the obviousness determination, the rejection is improper.

The compounds of the present invention have been rejected as obvious in view of compounds that are suggested in U.S. Pat. No. 5,075,487 ('487). However, the '487 patent teaches compounds that are useful as electron transport materials, and not as pharmaceutical agents. Although the compounds of the present invention are positional isomers of compounds that are suggested in the '487 specification (Col. 1, line 10 to column 2, line 4), the examiner presents no evidence that a person of ordinary skill in the

art of cancer treatment would be motivated to modify the compounds taught by the '487 patent to result in the instantly claimed compounds. There is no suggestion in the cited reference that the compounds taught therein would be useful for anything other than as intermediates useful for making electron transport materials. To rely on a reference as a basis for an obviousness rejection under § 103, it must be analogous prior art. *See, e.g.* M.P.E.P. § 2141.01.

The Federal Circuit has opined on the subject of analogous art and has decided that for purposes of determining whether a reference is analogous prior art, one of the following two inquiries must be met;

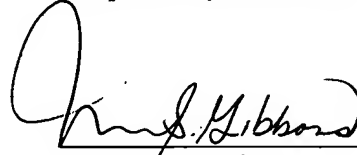
- (1) either the art is from the same field of endeavor, or
- (2) if the reference is not within the same field of the inventor's endeavor, the reference still is reasonably pertinent to the particular problem with which the inventor is involved.

See, In re Clay, 23 U.S.P.Q. 2d 1058, 1060 (Fed. Cir. 1992). Under the *Clay* test, the cited reference would not be considered analogous art because there is no connection whatsoever between electron transport materials useful for making electrophotographic photoreceptors and anticancer drugs. Thus, the examiner's reliance on the reference to support the rejection is unwarranted.

Furthermore, in determining patentability, the properties of any given compound must be considered together with the compound's structure. *See, In re Mehta*, 146 USPQ 284, 287 (CCPA 1065)(citing *In re Papesch*, 50 CCPA 1084). An implication of nonobviousness exists when the properties of a known compound vs. the properties of the claimed compound are different, if the property of the claimed compound is unexpected. 146 USPQ at 287 (discussing positional isomers). Here, the anticancer effect of the claimed compounds was certainly unexpected over the teachings of the '487 patent, and this evidences the nonobviousness of the claimed compounds.

For the foregoing reasons, Appellants respectfully request withdrawal of the obviousness rejection.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Maureen S. Gibbons", is written over a horizontal line.

Maureen S. Gibbons
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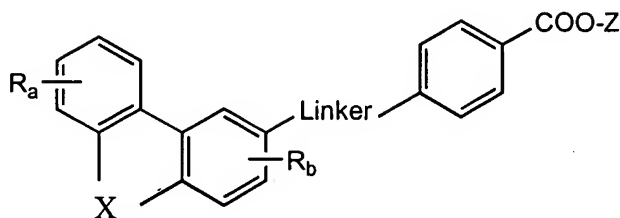
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Date: March 22, 2004

APPENDIX

In the claims:

- (Original) A compound represented by formula I



I

or a nontoxic pharmaceutically acceptable salt, physiologically hydrolyzable ester or solvate thereof, wherein

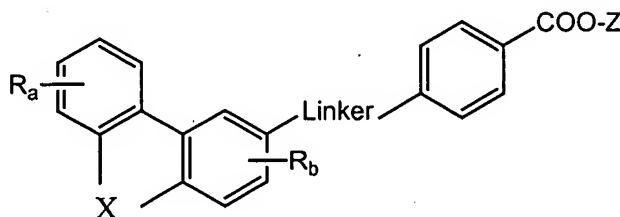
R_a and R_b are independently selected from the group consisting of hydrogen, halogen, hydroxy, nitro, amino, substituted amino, mercapto, polyfluoroalkyl, C_{1-6} alkyl, substituted C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylthio, formyl, carboxyl, aryl or heteroaryl;

Linker is selected from the group consisting of C_2 alkyl, C_2 alkenyl, C_2 alkynyl, $--C(=O)-NH--$, $--NH-C(=O)--$, $--CH_2O--$, $--O-C(=O)--$, $--C(=S)-NH--$, $--C(=O)-O--$, $--C(=O)-S--$, $--S-C(=O)--$, $--S-CH_2--$, $--CH_2-NH--$, $--C(=O)-CH_2--$, $--NH-C(=S)--$, $--CH_2S--$, $--OCH_2--$, $--NHCH_2--$;

X is O, S, $-C(R_1)_2$, $C=O$, $-C(R_1)_2Y--$ or $--YC(R_1)_2--$, wherein Y is selected from the group consisting of O, S and $C(R_2)_2$, wherein R_1 and R_2 are, independently, hydrogen or methyl; and

Z is hydrogen or C_{1-6} alkyl.

- (Original) A compound represented by formula I



or a nontoxic pharmaceutically acceptable salt, physiologically hydrolyzable ester or solvate thereof, wherein

R_a and R_b are independently selected from the group consisting of hydrogen, halogen, hydroxy, nitro, amino, mercapto, CF_3 , C_{1-6} alkyl, halosubstituted C_{1-6} alkyl, hydroxy-substituted C_{1-6} alkyl, aminosubstituted C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylthio, formyl, carboxyl, mono- or di- C_{1-6} alkyl-substituted amino, aryl or heteroaryl;

Linker is selected from the group consisting of $--CH=CH--$, $--C\equiv C--$, $--C(=O)-NH--$, $--NH-C(=O)--$, $--CH_2O--$, $--O-C(=O)--$, $--C(=S)-NH--$, $--C(=O)-O--$, $--C(=O)-S--$, $--S-C(=O)--$, $--S-CH_2--$, $--CH_2-CH_2--$, $--CH_2-NH--$, $--C(=O)-CH_2--$, $--NH-C(=S)--$, $--CH_2S--$, $--OCH_2--$, $--NHCH_2$ or $--CR_c=CR_d--$, wherein R_c and R_d are independently hydrogen or C_{1-6} alkyl;

X is O, S, $-C(R_1)_2$, $C=O$, $-C(R_1)_2Y--$ or $--YC(R_1)_2--$, wherein Y is selected from the group consisting of O, S and $C(R_2)_2$, and R_1 and R_2 are, independently, hydrogen or methyl; and

Z is hydrogen or C_{1-6} alkyl.

3. (Original) The compound of claim 2 wherein X is $--C(R_1)_2Y--$ or $--YC(R_1)_2--$, wherein Y is selected from the group consisting of O, S and $C(R_2)_2$ and R_1 and R_2 are, independently, hydrogen or methyl.

4. Cancelled

5. (Original) The compound of claim 3 wherein Linker is $--CH=CH--$ or $--C\equiv C--$.

Claims 6-9 cancelled

10. (Original) A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 and a pharmaceutically acceptable carrier therefor.

11. (Original) A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 2 and a pharmaceutically acceptable carrier therefor.

12. (Original) A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 3 and a pharmaceutically acceptable carrier therefor.

Claims 13-20 cancelled